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EXAMINER	
GUZO, D	

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☐ Responsive to communication filed on _____ ☑ This action is made final.

A shortened statutory period for response to this action is set to expire three(3) month(s), _____ ~~days~~ from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☑ Claims 39-60 are pending in the application.
   Of the above, claims 48 and 49 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 39-47 and 50-60 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

The restriction requirement made in Paper #4, and made FINAL in Paper #7, in the parent application S.N. 07/852390 is reiterated. Applicants' election with traverse of Group I in Paper No. 6 is reaffirmed and prosecution is being continued on the elected invention.

Claims 48 and 49 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 6.

This application contains claims 48 and 49 drawn to an invention non-elected with traverse in Paper No. 6. A complete response to the final rejection must include cancellation of non-elected claims or other appropriate action (37 C.F.R. § 1.144) M.P.E.P. § 821.01.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 39-47, 50, 51 and 55 are rejected under 35 U.S.C. § 103 as being unpatentable over Sanders et al. in view of Alberts et al.

Applicants recite a recombinant DNA sequence encoding the amino acid sequence of a hamster glutamine synthetase (GS) enzyme, a recombinant expression vector containing said GS sequence and a host cell transformed with said sequence.

Sanders et al. (AR, EMBO, Vol. 3, 1984, pp. 65-71, See whole document, particularly p. 69) recite the cloning of at least part of the hamster GS gene. Sanders et al. do not recite generation of an expression vector capable of expressing the GS gene or host cells transformed with said gene.

ALberts et al. ("Molecular Biology of the Cell", 1983, pp. 184-193) and Watson et al. ("Recombinant DNA, A Short Course", 1983, pp. 184-193) recite the generally routine steps of cloning a gene and expressing a cloned gene of interest in transformed host cells.

Applicants invention is essentially a logical conclusion to the work of Sanders et al. Applicants indeed recite that the methods used by Sanders et al. were duplicated in the instant disclosure (See Specification, Page 17, 2nd paragraph); therefore, given the teachings on preliminary identification of a portion of the GS gene (Sanders et al.) it must be considered that the subsequent cloning, sequencing and expression of the entire GS gene by following of the routine cloning and expression steps outlined by Alberts et al. and Watson et al. would have been obvious to an artisan of ordinary skill in the art. An

ordinary skilled artisan, seeking to isolate, clone and express an amplifiable gene, such as the GS gene, for potential use in coamplifying an additional foreign gene of interest, would have been motivated to use the teachings of Sanders et al. on a preliminary characterization and cloning of at least part of the GS gene combined with the routine steps of cloning, sequencing and expressing genes of interest in microorganisms recited by Alberts et al. and Watson et al. in order to isolate, clone and express the GS gene.

Claims 52-54 and 56-60 are rejected under 35 U.S.C. § 103 as being unpatentable over Sanders et al. in view of Alberts et al. or Watson et al. all further in view of Axel et al. (AA).

Applicants recite the use of a recombinant DNA vector comprising the amplifiable marker GS gene sequence and further comprising a second DNA sequence encoding a non-GS protein of interest, with said genes linked so as to result in amplification of the non-GS coding sequence. Applicants further recite the specific plasmids comprising the GS and tPA genes (pSVLGS.tPA16 and pSVLGS.tPA17), and use of recombinant plasmids comprising the GS gene to confer survivability to cells lacking adequate GS activity.

Sanders et al., Alberts et al. and Watson et al. are applied as above. Sanders et al., Alberts et al. and Watson et al. do not teach co-amplification of two different linked or un-linked DNAs.

Axel et al. (AA, U.S. Patent # 4399216, 8/16/83, See whole document, particularly the abstract and Column 3, 1st paragraph of "Summary" section, Column 5, last 2 paragraphs and Claim 54) recite the co-amplification of two different linked or un-linked DNAs, one DNA being an amplifiable gene coding for a dominant selectable marker such as drug resistance and the second DNA being a gene coding for a protein of interest.

Applicants invention is essentially an obvious variation on the teachings disclosed by Axel et al. It is noted that Axel et al. recite the linking, in a plasmid vector, of a dominant amplifiable, selectable, gene with a cloned gene of interest and the selection conditions for identification of cells which have acquired, amplified and expressed the selectable phenotype and hence the second cloned gene of interest. Therefore, an ordinary skilled artisan, seeking to amplify and express a gene of interest (e.g. tPA) by linking said gene to a dominant, amplifiable, selectable gene would have been motivated to use the teachings of Sanders et al. on the partial identification and cloning of the amplifiable dominant selectable GS gene combined with the teachings of Alberts et al. and Watson et al. on the routine steps involved in cloning, sequencing and expressing a gene of interest further combined with the teachings of Axel et al. on a method of amplifying and expressing a gene of interest by linking said gene to a dominant selectable gene (the GS gene would fall into this category) and selecting for cells containing

the two amplified genes under conditions suitable for survival of the cells containing the amplified dominant selectable gene in order to generate a recombinant vector with the dominant selectable amplifiable gene (GS) linked to a second gene of interest, transform suitable host cells (i.e. CHO-K1 cells) and culture cells under conditions which would permit selection of cells carrying the amplified genes. It would have been obvious to an ordinary skilled artisan, endeavoring to develop a procedure for amplification and expression of a gene of interest to use the teachings of Sanders et al. on the partial characterization of an amplifiable dominant selectable gene (GS) combined with the teachings of Alberts et al. and Watson et al. on the routine steps necessary to successfully clone, sequence and express a gene of interest further combined with the teachings of Axel et al. on the amplification and expression of genes of interest by linking said genes to amplifiable and selectable genes (e.g. GS) and selection of said gene combinations by culturing the transformed cells under selective conditions permitting survival of the cells which have acquired the gene combination in order to generate expression vectors (and transformed cells) comprising the GS gene and a gene encoding a protein of interest and culturing said transformed cells under conditions allowing for amplification and expression of said gene combinations.

The following is a quotation of the first paragraph of 35

U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention.

The plasmids pSLGS.tPA16 and pSVLGS.tPA17 are necessary for practicing of the instant invention in that these recombinant plasmids contain the DNA sequences coding for the GS gene, a foreign gene (tPA) and the sequences necessary for expression and/or amplification of said DNA. Given that the plasmids are essential for enablement of the invention and have not been described in sufficient detail to enable one of ordinary skill in the art to exactly duplicate said plasmids, a deposit of said plasmids is deemed necessary (See attachment on "Deposits of Biological Materials" supplied in Paper #7).

Claims 53 and 54 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 39 and 40 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to a hamster GS gene. See M.P.E.P. §§ 706.03(n) and 706.03(z). Applicants recite claims to recombinant DNA sequences encoding

mammalian or rodent GS genes but have enabled only the hamster GS gene and have not recited how one of ordinary skill in the art would go about isolating and identifying GS genes from any or all possible mammalian or rodent species. To identify GS genes from any mammal or rodent species it would be necessary to derive cell lines from that species (if they can be derived), select for mutants defective in GS activity (if they can be generated), isolate the regions of heterogeneity in the mutant and normal cell lines, fine map the sequences of interest, and finally determine if they encode a GS gene. Given these steps and the uncertainties inherent in each step, it is considered that undue experimentation would be required to practice the instant invention.

Claims 57 and 59 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to CHO-KI myeloma cells. See M.P.E.P. §§ 706.03(n) and 706.03(z).

It is unclear if myeloma cell lines can be generated from all mammalian species (Claim 57) or from any animal species (Claim 59). To practice the instant invention, an ordinary skilled artisan would need to generate myeloma cell lines from any animal or mammal species of interest. Given that myeloma cell lines have been isolated from only a few of the thousands of potential animal species in question, given the extensive diagnostic, clinical procedures and <u>in vitro</u> cell culture

techniques involved in identification, characterization, cloning and maintaining a new myeloma cell line and given that myeloma cell lines may not be able to be generated from all mammalian or animal species, it is considered that undue experimentation would be required to practice the instant invention.

Claim 44 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 44 is indefinite in that it is unclear what "high stringency conditions" encompass and it is unclear what DNA sequence comprises "a part thereof from a different species". The phrase "high stringency conditions" has potentially many different meanings and since applicants have not defined said conditions in the instant specification, it is unclear what conditions are encompassed by this term. Also, the phrase "a part thereof" potentially reads on the entire GS gene sequence minus one nucleotide down to a single nucleotide of the GS gene. The metes and bounds of the instant claim language need to be more precisely defined.

No claims are currently allowable in this application.

This is a FWC of applicant's earlier application S.N. 07/852390. All claims are drawn to the same invention claimed in

the earlier application and could have been finally rejected on the grounds or art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See M.P.E.P. § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (Nov. 16, 1993) and 1157 OG 94 (Dec. 28, 1993) (See 37 CFR 1.6(d)). The CM1 Fax Center number is (703) 305-3014. NOTE: If applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE

SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication should be directed to Examiner David Guzo at telephone number (703) 308-1906.

David Guzo

March 6, 1994

RICHARD A. SCHWARTZ
SUPERVISORY PATENT EXAMINER
ART UNIT 185